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EXAMINER

HARRIS, ALANA M

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 09/09/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/720,086

Applicant(s)

LI ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-10,13 and 24-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-10,13 and 24-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Response to Arguments and Amendments

1. Claims 1, 3-10, 13 and 24-37 are pending.
Claims 2, 11, 12 and 14-23 have been cancelled.
Claims 1, 8-10 and 13 have been amended.
Claims 1, 3-10, 13 and 24-37 are examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

3. Applicants have submitted amendments to the Sequence Listing to reflect the correct nucleotide and amino acid sequence contained in the deposited clones, ATCC Deposit Nos. 209933, 209934 and 98809, which corresponds to SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, respectively. Applicants aver that these clones were deposited prior to the filing of the provisional applications and accordingly Applicants' claims should be afforded the filing dates of the provisional applications.

These points of view have been carefully considered but found unpersuasive. Applicants have not presented corroborative evidence substantiating the fact that the deposited clones are the same as those disclosed in the PCT and provisional applications. There is insufficient proof suggestive that the proper sequences in the instant application and corresponding clones are one in the same as those listed in the

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priority documents. It still stands that sequences identical to SEQ ID NOS. 1-3 and 5-7 and there corresponding Figures are not found in PCT/US99/14373 (filed June 25, 1999), Provisional Applications number 60/090,906 (filed 6/25/1998) and 60/093,993 (filed July 24, 1998) and the corresponding figures. The priority date afforded to claims 1, 3-10 and 24-37 is the instant application's filing date of July 13, 2001. Accordingly, since the method of claim 13 now encompasses the polynucleotides of claim 1 it is also afforded the July 13, 2001 priority date.

Drawings

4. The drawings submitted with the originally filed application are objected to because of reasons cited on attached form PTO 948 completed by draftsman. Correction is required.

The marked up copy of drawings submitted in an effort to correct Figures 1A, 1B-1, 1C, 2B, 2C and 3A reflect changes to the sequences not supported by the priority documents. Additionally there was not corresponding clean copy submitted.

Withdrawn Objection

Specification

5. The disclosure is no longer objected to because of the brief description of the figures contain separate brief descriptions for the Figures.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

6. The rejection of claims 8, 9 and 13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants' arguments. Claim 2 has been cancelled.

Claim Rejections - 35 USC § 102

7. The rejection of claim 9 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,183,968 (effective filing date March 27, 1998) is withdrawn in light of the claim amendment. Claim 2 has been cancelled.
8. The rejection of claim 9 under 35 U.S.C. 102(b) as being anticipated by Accession number AF176228 (October 26, 1999) is withdrawn.

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9. The rejection of claims 8 and 10 under 35 U.S.C. 102(b) as being anticipated by Accession number AAT21884 of WO9514772 (June 1, 1995) has been withdrawn in light of the claim amendment.

10. The rejection of claims 8 and 10 under 35 U.S.C. 102(a) as being anticipated by Accession number AK025230 (September 20, 2000) is withdrawn.

New Grounds of Objection

Specification

11. The drawings originally filed with the specification are objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The material which is not supported by the original disclosure is as follows: Figures 1A, 1B-1, 1C, 2A, 2B, 2C, 3A and 3B which include changes to the nucleotide residues and nucleotide numbering. Furthermore, a clean copy did not accompany the marked up copy.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

12. Claim 1(f) is objected to because of the following informality: the term "polynucleotide" has been misspelled in both instances. Correction is required.

Maintained and New Grounds of Rejection

Claim Rejections - 35 USC § 112

13. Claims 8, 10 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have amended claim 8 to reflect that the isolated nucleic acid molecule comprising polynucleotides must have at least 50 contiguous nucleotides of SEQ ID NO: 1. Likewise, claim 10 has been amended to reflect that the isolated nucleic acid molecule comprising polynucleotides must have at least 100 contiguous nucleotides of SEQ ID NO: 3. Applicants state that support for these amendments are found *inter alia* at page 21, lines 7-25 of the specification. The Examiner has reviewed this section of the disclosure and does not concur with Applicants. Lines 7-25 of page 21 do not support that Applicants contemplated contiguous nucleotides of SEQ ID NO: 8 and 10 consisting of discrete fragments 50 and 100 nucleotides in length, respectively at the time of filing. Applicants are requested to remove the new matter or pointedly express where in the specification support can be found. Once the new matter is removed the art rejections previously of record in the first action on the merits (Paper number 12) reading on the claims will be reinstated.

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14. The rejection of claims 1, 3-10 and newly added claims 24-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants recite case law, as well as "...direct the Examiner's attention to Example 1 which describes...Applicants' cloning of mouse and human *de novo* cytosine methyltransferase genes and Applicants' extensive sequence analysis thereof." Applicants also aver that "[u]sing sequence alignments as a guide, the skilled artisan would be able to make predictions about which amino acids may be mutated for the protein to retain biological activity." Moreover, Applicants attest the approach by the Lazar reference cited by the Examiner differs from a potential infringer of Applicants' claims. These arguments and points of view have been carefully considered but found unpersuasive.

Applicants' specification does not provide sufficient guidance in the identification of which amino acid residues of the claimed polynucleotides are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved

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and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful. And as stated in the first action of the merits without guidance the changes which must be made in the nucleic acid sequences of SEQ ID NO: 1-4 to yield a full length protein commensurate to SEQ ID NO: 5-8 is not full-proof. Furthermore, the unidentified subfragments of SEQ ID NO: 1-4 are more than likely not to encode full-length polypeptides capable of *in vitro* methylation at the C5 position of cytosine in DNA. The specification continues to not provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acids in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

15. The rejection claims 1, 3, 4, 8, 9 and new claims 24-26, 29-33, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Okano et al. (Nature Genetics 19:219 and 220, July 19, 1998), as evidenced by Accession numbers AF068625, AF068626 and AF068627 (December 6, 1999) is maintained and made. Claim 2 has been cancelled.

"Applicants respectfully disagree[s] with ...the instant application's priority date [of]...July 13, 2001". Moreover, Applicants set forth that they are entitled to the priority date of June 25, 1998 and July 24, 1998 in view of the ATCC deposits made before the provisional filing dates. The Examiner's position on the instant application's priority has been made of record on page 2, paragraph 3 of the instant application. In essence

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claims 1, 3-10, 13 and 24-37 are afforded the effective filing date of the instant application, July 13, 2001.

Okano, as evidenced by Accession # AF068625 continues to read on amended claim 1, as well as claims 3 and 4 as set forth in the first action on the merits mailed January 14, 2003, page 7, paragraph 11. The claim language "a polynucleotide sequence complementary to the polynucleotide sequence" listed in claims 1 and 31 is given the broadest interpretation hence the prior art of record disclosing just one nucleotide sequence reads on the claims. Okano also discloses an isolated nucleic acid molecule that is at least 50 contiguous nucleotides of SEQ ID NO: 1. Accession numbers AF068626 and AF068627 disclose at least 30 contiguous nucleotides of SEQ ID NO: 2, as well as a subfragment thereof and a nucleotide sequence complementary to the said nucleotide sequence, see attached database sheet.

Given that the prior art polynucleotides are the same as that claimed it is reasonable to conclude that these polynucleotide encode a polypeptide capable of methylation at the C5 position of cytosine in DNA.

16. The rejection of claims 1, 3, 4, 8, 10 and new claims 24, 27-31, 34-37 under 35 U.S.C. 102(b) as being anticipated by Xie et al. (Gene 236(1): 87-95, 1999), as evidenced by Accession number AF067972 (February 12, 2001) is maintained and made. Claim 2 has been cancelled.

"Applicants respectfully disagree[s] with ...the instant application's priority date [of]....July 13, 2001". Moreover, Applicants set forth that they are entitled to the priority

date of June 25, 1998 and July 24, 1998 in view of the ATCC deposits made before the provisional filing dates. The Examiner's position on the instant application's priority has been made of record on page 2, paragraph 3 of the instant application. In essence claims 1, 3-10, 13 and 24-37 are afforded the effective filing date of the instant application, July 13, 2001.

Xie et al., as evidenced by Accession # AF067972 continues to read on amended claim 1, as well as claims 3 and 4 as set forth in the first action on the merits mailed January 14, 2003, page 8, paragraph 12. The claim language "a polynucleotide sequence complementary to the polynucleotide sequence" listed in claims 1 and 31 is given the broadest interpretation hence the prior art of record disclosing just one nucleotide sequence reads on the claims. Xie also discloses an isolated nucleic acid molecule that is at least 50 contiguous nucleotides of SEQ ID NO: 1 and at least 100 contiguous nucleotides of SEQ ID NO: 3.

Given that the prior art polynucleotides are the same as that claimed it is reasonable to conclude that these polynucleotide encode a polypeptide capable of methylation at the C5 position of cytosine in DNA.

17. The rejection of claim 13 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,492,168 (effective filing date April 22, 1998) is maintained.

Applicants argue that amended claim 13 has overcome the instant rejection and that the disclosing U.S. patent does not disclose the polynucleotides of claim 1. This argument has been considered but found unpersuasive.

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Claim 1 has been amended include limitations that broadly read on just one nucleotide sequence reads on the claims. U.S. Patent #6,492,168 discloses a nucleic acid sequence that is complementary to any one of SEQ ID NO: 5-8, which is capable of contacting DNA allowing for a method utilizing an expressed novel methyltransferase (M.CviPI) to methylate GpC *in vitro*, see column 18, lines 31-43 and column 20, lines 60-67. In a reaction mixture containing buffered solutions, cofactors, DNA substrate and M.CviPI the *in vitro de novo* methylation DNA assay was conducted. The DNA was investigated by purifying it from the reaction implementing an ethanol precipitation step.

Claim Rejections - 35 USC § 103

18. The rejection of claims 1, 3-10 and newly added claims 24-26, 29-33, 36 and 37 under 35 U.S.C. 103(a) as being unpatentable over Okano et al. (Nature Genetics 19:219 and 220, July 19, 1998), as evidenced by Accession number AF068625 (December 6, 1999) and Xie et al. (Gene 236(1): 87-95, 1999), as evidenced by Accession number AF067972 (February 12, 2001), in view of Ausubel et al. (Current Protocols in Molecular Biology 2, Unit 16.8, see pp.16.8.1-16.11.6) is maintained and made.

"Applicants respectfully disagree[s] with ...the instant application's priority date [of]....July 13, 2001". Moreover, Applicants set forth that they are entitled to the priority date of June 25, 1998 and July 24, 1998 in view of the ATCC deposits made before the provisional filing dates. The Examiner's position on the instant application's priority has been made of record on page 2, paragraph 3 of the instant application. In essence

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claims 1, 3-10, 13 and 24-37 are afforded the effective filing date of the instant application, July 13, 2001.

Okano and Xie are 102(b) anticipatory references that read on Applicants' claims. Accordingly these references can be combined with a secondary reference in order to establish a prima facie case of obviousness. The rejections are maintained for the reasons of record.

Conclusion

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ALANA HARRIS
PATENT EXAMINER



Alana M. Harris, Ph.D.
September 8, 2003